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A Minimal Polymer Model Integrates an Inverted Nuclear Geometry with Conventional Hi-C Compartmentalization MARTIN FALK, MIT, NATASHA NAUMOVA, UMass Medical, GEOFFREY FUDENBERG, MIT, YANA FEODOROVA, Medical University Plovdiv, MAXIM IMAKAEV, Harvard Medical, JOB DEKKER, UMass Medical, IRINA SOLOVEI, LMU Munich, LEONID MIRNY, MIT — The organization of interphase nuclei differs dramatically across cell types in a functionally-relevant fashion. A striking example is found in the rod photoreceptors of nocturnal mammals, where the conventional nuclear organization is inverted. In particular, in murine rods, constitutive heterochromatin is packed into a single chromocenter in the nuclear center, which is encircled by a shell of facultative heterochromatin and then by an outermost shell of euchromatin. Surprisingly, Hi-C maps of conventional and inverted nuclei display remarkably similar compartmentalization between heterochromatin and euchromatin. Here, we simulate a *de novo* polymer model that is capable of replicating both conventional and inverted geometries while preserving the patterns of compartmentalization as observed by Hi-C. In this model, chromatin is a polymer composed of three classes of monomers arranged in blocks representing constitutive heterochromatin, facultative heterochromatin, and euchromatin. Different classes of monomers have different levels of attraction to each other and to the nuclear lamina. Our results indicate that preferential interactions between facultative heterochromatin and constitutive heterochromatin provide a possible mechanism to explain nuclear inversion when association with the lamina is lost.

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